#### **Reviewer Report**

Title: The Gene Expression Deconvolution Interactive Tool (GEDIT): Accurate Cell Type Quantification from Gene Expression Data

**Version: Original Submission Date:** 9/10/2020

Reviewer name: Jian Hu

#### **Reviewer Comments to Author:**

â€"The authors present an algorithm called GEDIT using information from a reference dataset to estimate cell type abundances in a target dataset. This manuscript is not qualified to be published in the Giga Science because of the following reasons:

1. GEDIT does not show enough novelty.

As the authors stated in the response document, GEDIT has two key innovations: signature gene selection by information entropy and the row scaling step. As shown in Figure 2a, the signature gene selection only has a limited improvement than the others in terms of error. The authors also did not have enough evidence to support how and why the row scaling step is helpful. On top of these 2 data preprocessing steps, I did not find any innovations on the model of a non-negative linear regression.

2. GEDIT does not add much values in the field.

Although GEDIT is shown to have appealing results in comparison to existing methods on benchmarking experiments, it doesn't significantly outperform other methods in real data analysis in regards to Pearson correlation and average error. As demonstrated in Supplementary Figures 4 and 5, a main determinant of results quality for deconvolution is the reference used, not necessarily the algorithm.

3. I still think comparing GEDIT to other methods using single-cell RNA-seq as a reference is necessary. Utilizing single-cell RNA-seq for deconvolution becomes cutting-edge research and many tools have been designed for this purpose such as MuSic. These methods are proved to have superior performance using microarray as references and are commonly used. It is critical to demonstrate whether GEDIT has better performance than these methods.

## Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

### **Conclusions**

Are the conclusions adequately supported by the data shown? Choose an item.

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